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World Experience on COVID-19 Patients, Who Had Positive PCR for Nasal Swab and Underwent Surgical Interventions and Peritoneal Fluid Analysis for COVID-19

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1. Abstract

1.1. Aims: Aim of this literature review was to analyse the world experience on COVID-19 patients who underwent surgical intervention. Analyse the status of their peritoneal fluid and the surgical outcome in these COVID-19 patients.

1.2. Methods: Literature review of the published papers was performed over the last two years. The studies involving patients who had COVID -19 confirmed by PCR results of nasopharyngeal swabs and underwent a surgical procedure and had the peritoneal fluid samples examined to detect the presence of the COVID 19 virus.

1.3. Results: Ten papers assessing the COVID-19 in the peritoneal cavity were published, all of them were published in the year 2020. In all these studies total of 18 patients were confirmed COVID-19 on nasopharyngeal PCR and these were Assessed for the detection of the COVID-19 in the peritoneal cavity. Three patients (3/18, 16.6%) have no respiratory symptoms, fifteen (15/18, 83.33%) patients have respiratory symptoms. Seven patients (7/18, 38.8%) had COVID-19 detected in the peritoneum (Table 1), 2.dsa.

1.4. Conclusion: Patients with Respiratory symptoms are more likely to have peritoneal fluid positive for the disease. The overall mortality rate in patients with Pharyngeal PCR test +ve and who had surgical intervention is 9/18, 50%. Patients with Respiratory

symptoms and positive Nasopharyngeal PCR had mortality rate of 8/9, 88.88% among those who died in this group. It is difficult to comment on the mortality and morbidity of patients with COVID-19 in the peritoneal fluids as number of cases is small and many other variables can influence the morbidity and mortality in this group.

2. Introduction

The Corona virus causes respiratory infection, after 2-14 days of exposure symptoms like cough, fever, headache, myalgia and fatigue appear. Corona belongs to RNA family of viruses. Covid-19 is the new member of this family which surfaced in China in last months of 2019 [1]. During the early part of the COVID-19 pandemic new guidelines were formulated all over the world and implemented towards doctors, nurses, and healthcare workers in general, so that they can be protected from this life threatening infection while performing their duties in this COVID 19 pandemic. The surgical theatres working conditions, importantly theatre protocols have changed significantly which have financial and practical implications. The new rules were introduced in order to minimise exposure of viruses to surgeons, nurses and all other health care workers in the operation theatres. As a result of this it has resulted in the testing of patients and medical staff in the operation. The new guidelines were being quickly introduced and re updated rapidly to date by most international surgical societies,

to give surgical staff the most reliable and consistent guide lines while performing surgical cases which have potential or proved positive for COVID-19, especially in an emergency setting. [2, 3] It's important to mention here that when first wave of COVID-19 hit UK, all the elective surgeries except cancer surgeries were suspended in most places. The health care workers were compelled to work in situations of uncertainty and high risk for more than a year and this was due to lack of relevant data about viral load in the various body compartments and fluids. [4,5] The excretion path mechanisms of COVID-19 were mostly unknown. We believe that our review of available literature on this topic of "Potential Infectiousness of Peritoneal Secretions" will give important additional information from around the world on this burning topic which is still mystery for modern world of medical science [6].

3. Aim

Aim of this literature review was to analyse the world experience

on COVID-19 patients who underwent surgical intervention. Furthermore, to analyse the status of their peritoneal fluid and the surgical outcome in these COVID-19 patients.

4. Methodology

Literature review of the published papers was performed over the last two years. The studies involving patients who had COVID -19 confirmed by PCR results of nasopharyngeal swabs and underwent a surgical procedure and had the peritoneal fluid samples examined to detect the presence of the COVID 19 virus. Literature search was performed on Google and Pub Med using terms COVID19 with bowel perforation, Bowel ischemia in COVID, Peritonitis in COVID 19, COVID 19 and Acute abdomen, COVID in Surgical patients, COVID as Surgical emergency, COVID and PCR from peritoneal cavity fluid. Ten papers were identified which assessed the COVID-19 in the peritoneal cavity and which were published in the years 2020 and 2021 (Table 1).

Table 1: The published papers assessing peritoneal cavity and peritoneal fluid

	Date of publication	Corresponding author	Title
1	May 2020	S. Flemming	Abdominal fluid samples (negative for SARS-CoV-2) from a critically unwell patient with respiratory COVID-19
2	May 2020	Isaac José Felipe Corrêa Neto	Perforated acute abdomen in a patient with COVID-19: an atypical manifestation of the disease
3	May2020	Edoardo Rimini	COVID-19 in the peritoneal fluid: does this evidence oblige to introduce new rules? Presentation of a Case Report
4	Jun 2020	Barbara Seeliger	Is the severe Acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) present intraperitoneally in patients with coronavirus disease 2019 (COVID-19) infection undergoing emergency operations?
5	Jul 2020	Victor C Passarelli	Detection of SARS-CoV-2 in ascitic fluid: a case of viral peritonitis?
6	Jul 2020	A. Barberis	SARS-Cov-2 in peritoneal fluid: an important finding in the Covid-19 pandemic
7	Sep 2020	Saeed Safari	Detection of SARS-CoV-2 in Abdominal and Adipose Tissues
8	Sep 2020	Federico Coccolini	SARS-CoV-2 Is Present in Peritoneal Fluid in COVID-19 Patients
9	Sep 2020	Labib S. Al-Ozaibia	Splenic Abscess: An Unusual Presentation of COVID-19?
10	Sep 2020	Margarita Ibarra-Hernandez	Detection of SARS-CoV-2 in peritoneal fluid from patients with kidney disease and COVID-19: report of two cases

5. Results

Ten papers assessing the COVID-19 in the peritoneal cavity were published, all of them were published in the year 2020 (Table 1). Out of total 18 patients, 9 males and 9 females. Maximum age was 80 years and minimum age 30 years. Average age was 60.94 years (Table 1). In all these studies total of 18 patients were confirmed COVID-19 on nasopharyngeal PCR and these were assessed for the detection of the COVID-19 in the peritoneal cavity. Table 2.

Three patients (3/18, 16.6%) have no respiratory symptoms, fifteen (15/18, 83.33%) patients has respiratory symptoms (Table

2). Seven patients (7/18, 38.8%) had COVID-19 detected in the peritoneum (Table 2). Rectal swab was taken in 6 patients and it was positive in 5 of them. Fifteen patients underwent different surgical interventions and two patients had peritoneal dialysis for renal disease while one patient had Paracentesis. Eight patients of them (8/18, 44.4%) had varying degree of GI Ischemia and underwent surgical interventions for that. Seven Patients had surgeries for other diagnosis rather than GI Ischemia while two patients underwent surgical interventions post abdominal trauma (Table 2). In our study seven patients out of eighteen (7/18, 38.8%) had COVID-19 detected in the peritoneal cavity. All these eigh-

teen patients were also positive for COVID-19 on nasopharyngeal swab PCR test. It's important to mention that all the patient who were positive for Covid-19 in the peritoneal cavity has respiratory

symptoms as well 7/7, 100%. Which means patients with respiratory symptoms are more likely to have peritoneal fluid positive for the disease (Table 2).

Table 2: Analysis of the patient's demography, intervention, outcome and PCR results from nasopharyngeal as well as the peritoneum

Sex	Age	Diagnosis	Intervention	Outcome	Resp symptom	+ve PCR	+ve PCR
						N.pharngeal	peritoneum
1.Male	75	Liver cirrhosis	Paracentesis	Died day 10 post diagnosis	Yes	Yes	Yes
2.female	75	Empyema GB	Lap Chole	Died day 7post D	No	Yes	No
3.Male	39	Small bowel perforation	Resection and Anastomosis	D/C home day 5	No	Yes	No
4.Male	32	Gangrenous appendicitis	Lap Appendix	D/C day 4	No	yes	No
5.Male	30	Perforated duodenal ulcer	DU Repair	Died day 7	Yes	Yes	No
6.Male	30	Acute cholecystitis	Lap Cholecystectomy	Day 5 D/C	Yes	Yes	No
7.Male	56	Small bowel ischaemia	Resection& Anastomosis	Died	Yes	Yes	No
8.Female	71	Appendicitis	Lap Appendix	Died D4	Yes	Yes	No
9.Female	70	Sigmoid ischemia	Hartman's Procedure	D/C home D5	Yes	Yes	No
10.Male	44	Liver stab Haemo Peritoneum	Wash out	D3 D/C home	Yes	Yes	No
11.Female	70	Haemo Peritonem	Wash out	Died	Yes	Yes	No
12.Female	70	Intestinal bleeding	Subtotal Colectomy	Died day 7	Yes	Yes	Yes
13.Male	55	Splenic abscess	Laparotomy& Drainage	Died day16	Yes	Yes	No
14.Male	78	Small bowel obs/omental band	Adhesiolysis	D/C home D10	Yes	Yes	Yes
15.female	73	Umbilical hernia	Resection/ Anastomosis	D5 D/c home	Yes	Yes	Yes
16.Female	80	Sigmoid Perforation	Hartman's Procedure	Died D2	Yes	Yes	Yes
17.Female	71	End stage renal disease	Peritoneal Dialysis	D/C D8 home	Yes	Yes	Yes
18.Female	78	End stage renal disease	Peritoneal Dialysis	D/C D13 Home	Yes	Yes	Yes

The overall mortality rate in patients with Pharyngeal PCR test +ve only and who had surgical intervention is 9/18, 50%. However, of these 9 patients, 8/9 (88.88%) patients who died had Respiratory symptom and Pharyngeal PCR test +ve and whereas only 1/9 (11.11%) patients died who had no Respiratory symptoms but only Pharyngeal PCR test +ve. Which means that among patient who died and who had Respiratory Symptoms and Positive Nasopharyngeal PCR have mortality rate of 8/9, 88.88% in this group Table 2. Furthermore, it is observed that among the patients who died 3/9, 33.3% had Peritoneal fluid positive for PCR test. It is also observed that total of 7 patients had all 3 tests positive (i.e. Respiratory symptoms, Nasopharyngeal PCR & Peritoneal PCR positive) and out of them 3 died which makes mortality rate in this group 3/7, 42.8%. Table 2.

6. Discussion

The COVID-19 virus enters the cells through the Angiotensin Converting Enzyme-2 receptor, which is not only expressed in pneumocytes (type II alveolar cells), but also expressed in the epithelium of the gastrointestinal tract, from the oesophagus to the colon, notably in ileal and colonic enterocytes also [7]. The cell membrane protein Angiotensin-Converting Enzyme 2 is key for receptor-mediated cell entry of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) The GI tract can be damaged directly by the COVID-19 infection by the virus entry into the enterocytes or indirectly via the host inflammatory response [8]. The coronavirus through the tissue distribution, causes release of a high number of pro-inflammatory Cytokines which damages the micro vascular system, triggering abnormal activation of the coagulation system, which results generalized small-vessel vasculitis and extensive micro thrombi [9, 10]. This phenomenon, along with the patient's comorbidities, like hypertension and coronary disease, are linked with high mortality rates and a high risk of coagulation dysfunction.

The ischemia of the whole digestive tract with or without perforation reported may be the outcome of the septic and thromboembolic phenomena, resulted directly or indirectly by the viral infection. 44.4% (8/18 patients) of the reported cases had varying degrees of bowel Ischemia. Studies have revealed that critically ill patients with COVID-19 are more prone to have a Hypercoagulable state, with the outcome of intravascular coagulation due to local damage [11, 12]. Table-2 SARS-CoV-2 RNA has been isolated in the blood and faeces of COVID-19 patients [13, 14]. In our study five out six patients were tested positive when they had rectal swabs. Some authors have conducted studies on peritoneal fluid in COVID-19 positive patients, but without findings of the presence of the virus [15]. Table 2

The real-time reverse transcriptase-polymerase chain reaction used to identify the SARS-CoV-2 RNA genome in peritoneal fluid and nasal swabs. This identifies 3 targets, namely RNA-dependent

RNA polymerase, nucleoprotein (N), and envelope (E) [16]. The peritoneal fluid was detected positive and at levels comparable to the nasal swab and even when retested in 10-fold diluted [16]. This establishes that the viral load in the peritoneal fluid was higher compared to the upper respiratory samples and concluded that the surgical operation was indeed a procedure at risk of infection. Viral isolation, which would have provided stronger evidence of infectivity, could not be performed.

This expressed an important warning about the safety of the operating room staff and demanded an immediate update of the guidelines in order to protect surgical teams. Therefore, all the surgical procedures may risk the potential of aerosolization of the virus and the infection of the members of the surgical teams.

Laparoscopic or open surgical procedures both may result in gas/vapour forming manoeuvre. Operating devices like electro cautery, coagulation, and cutting devices produce gas and vapour which aerosolize the peritoneal fluid and consequently the virus. Activated *Corynebacterium*, human papillomavirus, hepatitis B virus, and human immunodeficiency virus have been detected in surgical smoke in the past [17]. Available literature has not shown direct relation between viremia and the severity of clinical picture. But in the presence of mild to moderate symptoms it is less likely to detect a positive viremia than in critically ill patients [18]. If we apply the same concept for the other body fluids, the greater the viremia, the higher the risks. As not much information available about the virus passage to peritoneal cavity and fluids, present data may suggest that potentially all people even those with mild to moderate respiratory symptoms by SARS-CoV-2 could present viral load in peritoneal fluid, thus increasing the exposure and contagion risks for the entire surgical staff. There are inadequate guide lines available to protect the theatre staff from contagion peritoneal fluid as there is not much data supporting potential risks of peritoneal fluids. Few guide lines have recently come up in the literature to help doctors, surgeons and theatre staffs in their daily practice [19].

All the surgical staff should be trained and educated about the potential risks of presence of COVID-19 in the peritoneal fluids and its potential to aerosolize to the environment from the peritoneal fluid in patients with SARS-CoV-2 [16].

7. Conclusion

Although there is limited data, but the percentages of detecting the COVID -19 in the peritoneum fluid is considerable. The overall mortality rate in patients with Pharyngeal PCR test +ve and who had surgical intervention is 9/18, 50%. Patients with Respiratory symptoms are more likely to get peritoneal fluid positive for the disease. Moreover patient who had Respiratory Symptoms and Positive Nasopharyngeal PCR have mortality rate of 8/9, 88.88% in this group Moreover it is difficult to comment on the exact mortality and morbidity of patients with COVID-19 in the peritoneal

fluids as number is small in this study and many other variables can influence the morbidity and mortality in this group. However, this review of the literature is very informative for surgeons and other theatre staff for increasing their level of awareness and protection especially in emergency surgical setting.

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